

WHAT IS CLAIMED IS:

1. An isolated polynucleotide encoding a STARS polypeptide.
- 5 2. The isolated polynucleotide of claim 1, wherein the STARS polypeptide comprises an amino acid sequence of SEQ ID NO:2, 4, 6, 8 or 10.
- 10 3. The polynucleotide of claim 1, wherein said polynucleotide has a nucleic acid sequence of SEQ ID NO:1, 3, 5, 7 or 9, or a complement thereof.
4. The polynucleotide of claim 2, wherein said polynucleotide further comprises a promoter operable in eukaryotic cells.
- 15 5. The polynucleotide of claim 4, wherein said promoter is selected from the group consisting of hsp68, SV40, CMV, MKC, GAL4_{UAS}, HSV and β-actin.
6. The polynucleotide of claim 5, wherein said promoter is a tissue specific promoter.
7. A nucleic acid of 15 to about 2000 base pairs comprising at least 15 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
- 20 8. The nucleic acid of claim 7, comprising 20 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
9. The nucleic acid of claim 7, comprising 25 contiguous base pairs of SEQ ID NO:1, 3, 5, 25 7 or 9, or the complement thereof.
10. The nucleic acid of claim 7, comprising 30 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.

11. The nucleic acid of claim 7, comprising 50 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
12. The nucleic acid of claim 7, comprising 100 contiguous base pairs of SEQ ID NO:1, 3, 5, 5 7 or 9 or the complement thereof.
13. The nucleic acid of claim 7, comprising 150 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
- 10 14. The nucleic acid of claim 7, comprising 250 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
- 15 15. The nucleic acid of claim 7, comprising 500 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
16. The nucleic acid of claim 7, comprising 1000 contiguous base pairs of SEQ ID NO:1, 3, 5, 7 or 9, or the complement thereof.
17. The nucleic acid of claim 7, comprising 2000 contiguous base pairs of SEQ ID NO:1, 2, 20 5, 7 or 9, or the complement thereof.
18. A peptide comprising 10 contiguous amino acids of SEQ ID NO:2, 4, 6, 8 or 10.
19. The peptide of claim 18, comprising 15 contiguous amino acids of SEQ ID NO:2, 4, 6, 8 25 or 10.
20. The peptide of claim 18, comprising 20 contiguous amino acids of SEQ ID NO:2, 4, 6, 8 or 10.
- 30 21. The peptide of claim 18, comprising 25 contiguous amino acids of SEQ ID NO:2, 4, 6, 8 or 10.

22. The peptide of claim 18, comprising 30 contiguous amino acids of SEQ ID NO:2, 4, 6, 8 or 10.

5 23. The peptide of claim 18, comprising 50 contiguous amino acids of SEQ ID NO:2, 4, 6 or 8.

24. An expression construct comprising a polynucleotide encoding a STARS polypeptide operably linked to a regulatory sequence.

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25. The expression construct of claim 24, wherein the polynucleotide encodes a STARS polypeptide comprising an amino acid sequence of SEQ ID NO:2, 4, 6, 8 or 10.

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26. The expression construct of claim 25, wherein said regulatory sequence is a tissue specific promoter.

27. The expression construct of claim 26, wherein said promoter is a muscle specific promoter.

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28. The expression construct of claim 27, wherein said muscle specific promoter is selected from the group consisting of myosin light chain-2 promoter, α actin promoter, troponin 1 promoter, $\text{Na}^+/\text{Ca}^{2+}$ exchanger promoter, dystrophin promoter, creatine kinase promoter, $\alpha 7$ integrin promoter, brain natriuretic peptide promoter, α B-crystallin/small heat shock protein promoter, α myosin heavy chain promoter and atrial natriuretic factor promoter.

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29. The expression construct of claim 25, wherein said promoter is an inducible promoter.

30. The expression construct of claim 25, wherein said expression construct is contained in a viral vector.

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31. The expression construct of claim 25, wherein said viral vector is selected from the group consisting of a retroviral vector, an adenoviral vector, and adeno-associated viral vector, a vaccinia viral vector, a herpesviral vector, a polyoma viral construct or a Sindbis viral vector.

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32. The expression construct of claim 24, wherein said expression construct comprises a polyadenylation signal.

10 33. The expression construct of claim 24, wherein said expression construct comprises a second polynucleotide encoding a second polypeptide.

34. The expression construct of claim 32, wherein said second polynucleotide is under the control of a second regulatory sequence.

15 35. A polypeptide comprising the sequence of SEQ ID NO:2, 4, 6, 8 or 10.

36. A method of screening for modulators of STARS expression comprising:

20 (a) providing a cell in which a STARS promoter directs the expression of a polypeptide;
(b) contacting said cell with a candidate modulator; and
(c) measuring the effect of said candidate modulator on said polypeptide,

25 wherein a difference in expression of said polypeptide, as compared to an untreated cell, indicates that said candidate modulator is a modulator of STARS expression.

37. The method of claim 36, wherein measuring comprises Northern analysis.

38. The method of claim 36, wherein measuring comprise PCR.

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39. The method of claim 36, wherein measuring comprises RT-PCR.

40. The method of claim 36, wherein measuring comprises immunologic detection of STARS.

5 41. The method of claim 36, wherein measuring comprises ELISA.

42. The method of claim 36, wherein measuring comprises immunohistochemistry.

43. The method of claim 36, wherein said cell is located in an animal.

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44. The method of claim 36, wherein said cell is a myocyte.

45. The method of claim 44, wherein said cell is a cardiomyocyte.

15 46. The method of claim 36, wherein said modulator decreases expression of the polypeptide.

47. The method of claim 36, wherein said modulator increases expression of the polypeptide.

48. The method of claim 36, wherein said polypeptide is STARS.

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49. The method of claim 36, wherein said polypeptide is a screenable marker polypeptide.

50. The method of claim 49, wherein said screenable marker polypeptide is luciferase, β -galactosidase, CAT or green fluorescent protein.

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51. A method of screening for modulators of STARS actin-binding activity comprising:

(a) providing an active STARS preparation;

(b) contacting said STARS preparation with a candidate modulator; and

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(c) measuring the actin binding activity of said STARS preparation,

wherein a difference in actin binding activity of said STARS preparation, as compared to an untreated STARS preparation, indicates that said candidate modulator is a modulator of STARS actin binding activity.

5 52. The method of claim 51, wherein said method is performed in a cell free assay.

53. The method of claim 51, wherein said method is performed in a cell.

54. The method of claim 51, wherein binding is determined by chromatographic separation.

10 55. The method of claim 51, wherein binding is determined by electrophoretic separation.

56. A method of screening for an inhibitor of STARS-induced transcription comprising:

15 (a) providing a cell that expresses STARS and contains a STARS-regulated promoter linked to an indicator gene;

(b) contacting said cell with a candidate modulator; and

(c) measuring the effect of said candidate modulator on expression of said indicator gene,

20 wherein a difference in expression of said indicator gene, as compared to an untreated cell, indicates that said candidate modulator is a modulator of STARS-induced transcription.

57. The method of claim 56, wherein said cell is a myocyte.

25 58. The method of claim 56, wherein said cell is a cardiomyocyte.

59. The method of claim 56, wherein said STARS-regulated promoter is *SM22*.

60. The method of claim 56, wherein said indicator gene encodes luciferase, β -galactosidase, CAT or green fluorescent protein.

61. A method of producing a STARS polypeptide in a cell comprising:

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- (a) transforming a cell with an expression cassette comprising a nucleic acid encoding STARS under the control of a promoter active in said cell;
- (b) culturing said cell under conditions suitable for expression of STARS.

10 62. The method of claim 61, wherein said cell is a cardiomyocyte or a fibroblast, such as a cardiac fibroblast.

63. The method of claim 61, wherein said cell is located in an animal.

15 64. The method of claim 61, wherein transforming comprises infection with a viral vector.

65. The method of claim 61, wherein transforming comprises contacting of said cell with a liposome comprising said expression cassette.

20 66. The method of claim 61, wherein transforming comprises electroporation, calcium phosphate precipitation or protoplast fusion.

67. The method of claim 61, wherein said cell is a prokaryotic cell.

25 68. The method of claim 61, wherein said cell is a eukaryotic cell.

69. The method of claim 61, further comprising the step of purifying said STARS polypeptide away from other cellular components.

30 70. A non-human transgenic animal comprising a selectable or screenable marker protein under the control of a STARS promoter.

71. A non-human transgenic animal comprising a STARS encoding nucleic acid under the control of an inducible promoter.

5 72. A non-human transgenic animal comprising a STARS encoding nucleic acid under the control of a constitutive promoter.

73. A non-human transgenic animal lacking at least one STARS allele.

10 74. The non-human transgenic animal of claim 73, wherein said animal lacks both alleles of STARS.

75. A method of inhibiting STARS activity comprising contacting a cell expressing STARS with a compound that inhibits STARS activity.

15 76. The method of claim 75, wherein said compound is a nucleic acid antisense to a STARS regulatory or coding region.

77. The method of claim 75, wherein said compound is a ribozyme that selectively cleaves a 20 STARS transcript.

78. The method of claim 75, wherein said compound is a small molecule inhibitor.

79. The method of claim 75, wherein said compound is a single chain antibody that binds 25 immunologically to STARS.

80. A method of treating cardiac hypertrophy and dilated cardiomyopathy comprising decreasing STARS activity in heart cells of a subject.

81. The method of claim 80, wherein STARS activity is decreased by delivering an expression vector comprising a polynucleotide encoding an antisense STARS construct, a STARS ribozyme or an anti-STARS single-chain antibody to said subject.

5 82. The method of claim 81, wherein the expression vector is a non-viral vector.

83. The method of claim 81, wherein the expression vector comprises a viral vector.

10 84. The method of claim 83, wherein said viral vector is an adenoviral construct, a retroviral construct, an adeno-associated viral construct, a herpesviral construct, a vaccinia viral construct, a polyoma viral construct or a Sindbis viral vector.

15 85. The method of claim 84, wherein the viral vector comprises a replication-defective adenovirus.

86. The method of claim 81, wherein the step of delivering the expression construct comprises introducing a viral vector comprising the nucleic acid into the heart of the mammal by direct injection into the heart tissue.

20 87. The method of claim 81, wherein the step of delivering the expression construct comprises introducing the expression construct into the lumen of at least one vessel supplying blood to the heart.

25 88. The method of claim 81, further comprising administering a second anti-hypertrophic drug to said subject.

89. A method of treating myocardial infarct comprising decreasing STARS activity in heart cells of a subject.

30 90. A method of preventing cardiac hypertrophy and dilated cardiomyopathy comprising decreasing STARS activity in heart cells of a subject.

91. A method of inhibiting progression of cardiac hypertrophy comprising decreasing STARS activity in heart cells of a subject.

5 92. A method of treating heart failure comprising decreasing STARS activity in heart cells of a subject.

93. A method of inhibiting progression of heart failure comprising decreasing STARS activity in heart cells of a subject.

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94. A method of increasing exercise tolerance in a subject with heart failure or cardiac hypertrophy comprising decreasing STARS activity in heart cells of a subject.

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95. A method of reducing hospitalization in a subject with heart failure or cardiac hypertrophy comprising decreasing STARS activity in heart cells of a subject.

96. A method of improving quality of life in a subject with heart failure or cardiac hypertrophy comprising decreasing STARS activity in heart cells of a subject.

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97. A method of decreasing morbidity in a subject with heart failure or cardiac hypertrophy comprising decreasing STARS activity in heart cells of a subject.

98. A method of decreasing mortality in a subject with heart failure or cardiac hypertrophy comprising decreasing STARS in heart cells of a subject.

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99. A method of producing a modulator of STARS expression comprising:

(a) providing a cell in which a STARS promoter directs the expression of a polypeptide;

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(b) contacting said cell with a candidate modulator;

- (c) measuring the effect of said candidate modulator on said polypeptide, wherein a difference in expression of said polypeptide, as compared to an untreated cell, indicates that said candidate modulator is a modulator of STARS expression; and
- (d) producing said modulator.

100. A method of producing a modulator of STARS actin binding activity comprising:

- (a) providing an active STARS preparation;
- (b) contacting said STARS preparation with a candidate modulator;
- (c) measuring the actin binding activity of said STARS preparation, wherein a difference in actin binding activity of said STARS preparation, as compared to an untreated STARS preparation, indicates that said candidate modulator is a modulator of STARS actin binding activity; and
- (d) producing said modulator.

101. A modulator of STARS expression identified according to the method comprising:

- (a) providing a cell in which a STARS promoter directs the expression of a polypeptide;
- (b) contacting said cell with a candidate modulator; and
- (c) measuring the effect of said candidate modulator on said polypeptide,

wherein a difference in expression of said polypeptide, as compared to an untreated cell, indicates that said candidate modulator is a modulator of STARS expression.

102. A modulator of STARS actin binding activity identified according to the method comprising:

- (a) providing a STARS preparation;
- (b) contacting said STARS preparation with a candidate modulator; and

(c) measuring the actin binding activity of said STARS preparation,

wherein a difference in actin binding activity of said STARS preparation, as compared to an untreated STARS preparation, indicates that said candidate modulator is a modulator of STARS actin binding activity.

5 103. An antibody that binds immunologically to STARS.

104. A polyclonal antibody preparation, antibodies of which bind immunologically to STARS.

105. A hybridoma cell that produces a monoclonal antibody that binds immunologically to STARS.